methods for diagnosing colon cancer, and are thus inapposite to the instant claims, which do not refer to methods of diagnosis. The amendments are supported at least at page 2, lines 16-20, page 4 lines 18-26, page 35 line 28-page 36 line 7, and Figure 2. Figure 2 and page 35 line 28-page 36 line 7 in particular demonstrate the increased risk of developing colon cancer at an age less than about 35 resulting from the presence of at least one alanine substitution at position -9 in the MTS. The absence of statistically significant results in the small non-Hispanic population studied is simply a result of sample size, but similar results can reasonably be expected following the teachings of this application based on the results obtained from the working example Hispanic subpopulation for which a statistically significant number of young colon cancer patients were present in the sample. This working example demonstrates the enablement of the teachings in the application.

The claims are therefore asserted to be fully enabled. The Examiner is respectfully requested to withdraw the rejections under 35 U.S.C. § 112, first paragraph.

B. **35 U.S.C. § 112, First Paragraph, Written Description**

Claims 14-31 were rejected as not sufficiently described in the specification. The Examiner objected to the terms "assigning an intermediate risk" and "early onset colorectal cancer" as not explicitly supported in the application. The support for the claim language is recited above, and was recited in the prior amendment. *Ipsis verbis* support is not required for claim language, and it is well established that all parts of the application, including the Figures, can provide support for claim terms. See MPEP 2163; *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991).

Nevertheless, the claims have been amended to recite language explicitly found in the application due to the procedural posture of the case. Specifically, see Figure 2 showing the age distribution of colorectal cancer patients as compared to their genotype. See also p. 2. lines 16-21, reciting a method of determining colorectal cancer susceptibility "wherein a patient with one or two alleles encoding alanine at position -9 of the MnSOD signal peptide has an increased risk of developing colorectal cancer." See also p. 4, esp. lines 24-26, teaching "The invention is based on the discovery that Ala/Ala individuals are likely to develop colorectal cancer at a younger age compared to Ala/Val individuals who, in turn, are likely to develop colorectal cancer at a younger age compared to Val/Val individuals." See also p. 35 line 30-p. 36 line 2:

"Patient's homozygous for the alanine allele (24/64) showed a mean age of 37.6 years compared to 42.3 years for heterozygotes (29/64) and 48.4 years for patients homozygous for the V allele (11/64) (p=0.045, see figure 2)." See also claim 29 as filed. See also p. 20, lines 20-23: "When the age of the subject is less than 35 years and the base identity at position 351 is homozygous for C or heterozygous, the subject's risk for developing colorectal cancer is assessed to be greater than that of the unaffected relevant population."

As the claims are fully supported by the description in the specification, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph is respectfully requested.

C. **35 U.S.C. § 112, Second Paragraph**

Claims 27-30 were rejected as indefinite based on the recitation of two terms, both of which involved antecedency issues. The additional terms or phrases to which the Examiner objected have been deleted or amended to address the Examiner's concerns. The Examiner is therefore respectfully requested to withdraw the rejections under 35 U.S.C. § 112, second paragraph.

CONCLUSION

Applicants respectfully request reconsideration of the claims in view of the above amendments and remarks. A notice of allowance is earnestly solicited. If a telephone conference would expedite allowance of this matter, the Examiner is welcome to contact the undersigned at (650) 849-4908.

If an appropriate payment does not accompany or precede this submission, the Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§ 1.16 and 1.17, including any petition for extension of time, or to credit any overpayment, to Deposit Account No. 50-2518, docket number 13761-7001.

NOTICE OF FIRM NAME CHANGE

Agent for Applicant wishes to inform the Office that the name of its firm has been changed to Bingham McCutchen LLP.

DATE: March 20, 2003

Respectfully submitted,

By: _____

David W. Maher
Registration No.: 40,077

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Response to 11/20/02 Office Action
13761-7001

14. (Amended) The method of claim ~~21~~ 31 comprising contacting a sample of the subject's nucleic acid comprising the MnSOD gene with a probe or primer which can hybridize to a region of the MnSOD gene encoding the MTS, said region including nucleotide 351 of SEQ ID NO:1.

15. (Amended) The method of claim 31, wherein determining whether ~~an~~ a first and/or second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises determining the identity of at least one nucleotide of the region encoding the MTS.

16. (Amended) The method of claim 31, wherein determining whether ~~an~~ a first and/or second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises performing a restriction enzyme site analysis.

17. (Amended) The method of claim 31, wherein determining whether ~~an~~ first and/or second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises performing a single-stranded conformation polymorphism analysis.

18. (Amended) The method of claim 31, wherein determining whether ~~an~~ first and/or second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises performing an allele specific hybridization.

19. (Amended) The method of claim 31, wherein determining whether ~~an~~ first and/or second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises performing a primer specific extension.

20. (Amended) The method of claim 31, wherein determining whether ~~an~~ first and/or second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises performing an oligonucleotide ligation assay.

Please cancel claims 21 and 29-30.

22. The method of claim 14, wherein the probe or primer has a nucleotide sequence from about 15 to about 30 nucleotides.

23. The method of claim 31, wherein the probe or primer is labeled.

24. (Amended) The method of claim ~~21~~31, wherein ~~determining whether an allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS comprises determining the base identity of a portion of genomic DNA from a sample from the subject, said genomic DNA comprising an MnSOD gene comprising a coding region for the mitochondrial targeting sequence, said portion corresponding to position 351 as defined in SEQ ID NO:1 of said MnSOD gene in said mitochondrial targeting sequence.~~ determining whether said first and/or second allele of the MnSOD gene comprise a mutation in the coding region for the MTS comprises analyzing the genomic DNA of said subject.

25. (Amended) The method of claim 2431; wherein ~~the base identity of said portion is determined by~~ determining whether said first and/or second allele of the MnSOD gene comprise a mutation in the coding region for the MTS comprises sequencing.

26. (Amended) The method of claim 24; wherein ~~the base identity of said portion is determined by~~ determining whether said first and/or second allele of the MnSOD gene comprise a mutation in the coding region for the MTS comprises digesting said ~~portion~~ genomic DNA with an appropriate restriction endonuclease.

27. (Amended) The method of claim ~~24~~31; wherein ~~said base identity is determined by examining an RNA fraction from said subject's sample, whereby the identity of said genomic DNA at said position 351 can be determined.~~ determining whether said first and/or second allele of the MnSOD gene comprise a mutation in the coding region for the MTS comprises analyzing the RNA of said subject.

28. (Amended) The method of claim 24; wherein the mutation in the coding region for the MTS resulting in a loss of α-helical structure in the MTS is a C at ~~said~~ a position corresponding to position 351 in SEQ ID NO:1.

31. (Amended) A method of determining relative age-related risk of colorectal cancer in a Hispanic subject ~~susceptible thereto~~, comprising:

determining whether a first and/or second allele of a manganese superoxide dismutase (MnSOD) gene in the subject comprises a mutation in the coding region for the mitochondrial targeting sequence (MTS) of the MnSOD protein resulting in a loss of α-helical structure in the MTS;

~~determining whether a second allele of the MnSOD gene in the subject comprises a mutation in the coding region for the MTS of the MnSOD protein resulting in a loss of α-helical structure in the MTS;~~

assigning a lower risk of developing ~~early onset~~ colorectal cancer at an age of less than about 35 years to ~~a~~ said subject ~~having~~ when the subject has no mutation in either the first or second allele of the MnSOD gene resulting in a loss of α-helical structure in the MTS; and

assigning a higher risk of developing ~~early onset~~ colorectal cancer at an age of less than about 35 years to ~~a~~ said subject ~~having~~ when the subject has mutations in one or both the first and second alleles of the MnSOD gene resulting in a loss of α-helical structure in the MTS; ~~and~~

~~assigning an intermediate risk of developing early onset colorectal cancer to a subject having a mutation in only one of the first and second allele of the MnSOD gene resulting in a loss of α-helical structure in the MTS~~

wherein determining whether said first and/or second allele of the MnSOD gene comprise a mutation in the coding region for the MTS comprises determining whether said first and/or second allele encodes an alanine at position -9 of the MnSOD signal peptide.